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**TRANSMITTAL
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Application Number

09/361,652

Filing Date

July 27, 1999

First Named Inventor

Zuker, Charles S.

Art Unit

1649

Examiner Name

Michael T. Brannock

Attorney Docket Number

02307E-088610US

ENCLOSURES (Check all that apply)☐

Fee Transmittal Form

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Fee Attached

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Amendment/Reply

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After Final

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Affidavits/declaration(s)

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After Allowance Communication to TC

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(Appeal Notice, Brief, Reply Brief)
Appellant's Reply Brief w/Exhibit A☐

Proprietary Information

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Application☐Reply to Missing Parts
under 37 CFR 1.52 or 1.53

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Chuan Gao

Date

December 11, 2007

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54,111

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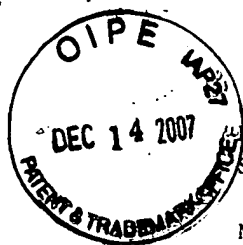
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TOWNSEND and TOWNSEND and CREW LLP

By:

Malinda Wajit

PATENT

Attorney Docket No.: 02307E-088610US

DHHS Ref. No. E-003-99/0

U.C. Ref. No. 98-306-2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Zuker et al.

Application No.: 09/361,652

Filed: July 27, 1999

For: NUCLEIC ACIDS ENCODING A
G-PROTEIN COUPLED RECEPTOR
INVOLVED IN SENSORY
TRANSDUCTION

Customer No.: 20350

Confirmation No. 5785

Examiner: ULM, John D.

Technology Center/Art Unit: 1649

APPELLANT'S REPLY BRIEF UNDER 37
C.F.R. §41.41

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This brief is filed pursuant to 37 C.F.R. §41.41, in response to the Examiner's Answer mailed October 18, 2007. A Request for an Oral Hearing is NOT filed.

I. Overview

Claims 1, 4-6, 8, 34, 35, and 61-67 stand rejected under 35 U.S.C. §101 for alleged lack of patentable utility and under 35 U.S.C. §112, first paragraph, for alleged lack of enablement due to lack of utility. These claims relate to a nucleic acid encoding a taste transduction G-protein coupled receptor, GPCR-B3, which is expressed specifically in taste cells. It is asserted in the specification that GPCR-B3 is involved in taste perception, and that GPCR-B3 polypeptides or the encoding nucleic acids can be used to identify taste cells, to generate taste topographic map, and to provide a screening method for compounds that modulate taste signaling. During prosecution, Appellant submitted a declaration under 37 C.F.R. §1.132 by inventor Dr. Zuker and also relied on the publication by Nelson *et al.* to support the asserted utility of GPCR-B3. In contrast, the Examiner has repeatedly maintained the utility rejection and utility-based enablement rejection without relying on any objective evidence.

In the sections below, Appellant will individually address the specific points raised in the Examiner's Answer of October 18, 2007..

II. The Nelson Reference Establishes GPCR-B3 as a Taste-Regulating Protein

In the Examiner's Answer mailed October 18, 2007, the Examiner maintains the utility rejection and utility-based enablement rejection, arguing that, although an artisan would recognize GPCR-B3 as a G-protein coupled receptor specifically expressed in taste cells, the protein "does not correspond to a known protein having an established role in the perception of taste" (page 4 of the Examiner's Answer). The Examiner further states that GPCR-B3 has no practical utility unless it is shown which of the sensation, sweet, bitter, sour, salty, and/or unami, are induced by this protein (pages 5-6 of the Examiner's Answer). Appellant respectfully disagrees with the Examiner.

As an initial matter, Appellant reiterates that, according to the MPEP and case law, the burden rests with the Examiner to "set forth factual reasons which would

lead one skilled in the art to question objective truth of the statement of operability" and that the Examiner cannot simply dismiss an asserted utility as "wrong," "even when there may be reason to believe the assertion is not entirely accurate" (MPEP §2107.02 IV). The Examiner has admittedly relied on no objective evidence to challenge the asserted utility (page 3 of the Examiner's Answer), yet continues to argue that "[t]here is absolutely no evidence of record or any line or reasoning that would support a conclusion that a protein of the instant invention is involved in taste perception in general" (page 7 of the Examiner's Answer). Such arguments directly contradict the MPEP.

Secondly, even assuming the Examiner had a established *prima facie* case of lack of patentable utility, Appellant believes that it would be sufficiently rebutted by additional evidence offered by Appellant by way of Dr. Zuker's declaration and the Nelson reference. Dr. Zuker attests in his declaration that, given the state of the art and the disclosure of this application, one of skill in the art would find the asserted utility of GPCR-B3 as specific, substantial, and credible. The Nelson reference, published after the filing date of this application, confirms the utility of GPCR-B3 as asserted in this application by demonstrating that the protein (also known as T1R1) forms a heterodimer with T1R3 and participates in the taste perception of L-amino acids, which are known to impart different tastes, depending on the individual amino acid (see, *e.g.*, one exemplary web search result shown in **Exhibit A**).

Since the Examiner again offers no evidence to rebut the declaration and the Nelson reference, Appellant believes that all evidence of record is in favor of a holding of sufficient utility.

III. The Examiner Has Applied Inappropriate Utility Requirement for the Claimed Subject Matter

On page 6 of the Examiner's Answer, the Examiner contends that, because the specification does not identify a particular physiological process regulated by GPCR-B3, "an artisan would have no way of knowing what effects the administration of a ligand

(GPCR-B3 modulator) to an organism would have," and that identification of the ligand (GPCR-B3 modulator) would therefore convey no benefit to the public. Appellant does not agree with this reasoning.

To begin with, Appellant contends that at least one particular physiological process regulated by GPCR-B3 is indeed identified in the specification and confirmed by the Nelson reference: GPCR-B3 participates in taste perception, especially the perception of L-amino acids. As shown in Exhibit A, it is well known that different amino acids can have sour, unami, sweet, or bitter taste.

The Examiner has also applied incorrect legal standards when considering the utility of the subject matter claimed in this application. The pending claims are drawn to a nucleic acid encoding a GPCR-B3 polypeptide, not a GPCR-B3 modulator. Although the utility of the GPCR-B3 polypeptide (and its coding sequence) is asserted, in one aspect, through the use of its modulators, Appellant does not believe that the same set requirements for should apply to the GPCR-B3 nucleic acid/polypeptide claims and to the GPCR-B3 modulator claims, insofar as patentability is concerned regarding, for example, utility, enablement, and written description. The Examiner has over-emphasized the significance of the exact effect of a GPCR-B3 modulator on taste perception, in essence applying to the GPCR-B3 nucleic acid claims the utility and enablement requirements for the GPCR-B3 modulator claims. Appellant contends that it is inappropriate.

Furthermore, even for a claim directed to a GPCR-B3 modulator, a patent application need not reveal the identity of a specific signaling pathway regulated by GPCR-B3 and therefore by the GPCR-B3 modulator in order to meet the utility, written description, and enablement requirements. Indeed, our patent law requires the disclosure of a useful invention that works, but does not require a patent applicant to illustrate the mechanism of action through which his invention works.

As such, neither the alleged lack of disclosure of a physiological process regulated by GPCR-B3 nor the alleged lack of disclosure of the exact effect of a GPCR-B3 modulator provides a valid basis for maintaining the utility rejection.

IV. One Utility Is Sufficient for 35 U.S.C. §101

On pages 8-10 of the Examiner's Answer, the Examiner argues that the asserted utility of GPCR-B3 as a paternity or forensic marker is neither specific nor substantial. Analogizing the asserted utility of GPCR-B3 as a tissue marker with the use of any given protein as an analytical standard, such as a molecular weight marker, the Examiner also argues that the use of GPCR-B3 as a tissue marker is not a specific or substantial utility.

In response, Appellant first points out that, for the purpose of satisfying the requirement under 35 U.S.C. §101, an invention only needs to have one utility. As already established by the Nelson reference and Dr. Zuker's declaration (which is not rebutted by the Examiner), GPCR-B3 is a taste cell specific GPCR involved in taste perception and its modulators can in turn modulate how tastes are perceived. One utility of the GPCR-B3 polypeptide/nucleic acid is therefore to identify compounds useful for modulating tastes. Since this utility alone is sufficient to meet the requirement under 35 U.S.C. §101, whether or not GPCR-b3 has other patentable utility is simply irrelevant.

Secondly, the use of GPCR-B3 as a tissue marker for the purpose of identifying taste cells or generating a taste topographic map is a specific and substantial utility. As explained in the declaration by Dr. Zuker, given the structure and expression pattern of GPCR-B3, as well as the results of a functional assay using a chimeric GPCR construct, one of skill in the art would reasonably recognize the use of GPCR-B3 polypeptide or nucleic acid for identifying taste cells and to generate taste topographic map. Appellant contends that these uses are applicable to a taste cell specific protein only and are therefore specific, which is clearly distinguished from the truly generic use (such as a molecular weight marker) that any protein can provide. Since the Examiner

offers no evidence or objective reasoning to rebut Dr. Zuker's declaration, Appellant submits that this point is established for the record.

In short, even if successful, the Examiner's attack on the asserted utility of GPCT-B3 as a paternity marker, a forensic marker, or a tissue-specific marker, does not negate patentable utility of GPCR-B3 under 35 U.S.C. §101.

V. Summary

In summary, the Examiner has neither carried his initial burden to establish a *prima facie* case of lack of patentable utility, nor has he rebutted the evidence presented by way of the Nelson publication and Dr. Zuker's declaration supporting the asserted utility. Furthermore, the Examiner has relied on flawed logic and applied incorrect legal standards in assessing the utility question of this invention. As such, Appellant contends that the utility rejection and utility-based enablement rejection are improper and respectfully requests their reversal.

Respectfully submitted,



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Attachment (Exhibit A)
CG:cg
61213247 v1

Exhibit A



Let's learn
about amino acids!

- What are amino acids?
- 20 kinds of amino acids
that support the body

→ Q&A

→ For more
about amino acids

→ Production process

How versatile
amino acids are!

⇒ FOOD

→ SPORTS

→ HEALTH

→ MEDICAL CARE

→ BEAUTY CARE

How versatile amino acids are!

FOOD and amino acids

- ☑ Vine-ripened tomatoes
- ☑ Crabs and sea urchins
- ☑ fermented food
- ☑ Sweetness that does not make you fat

Amino acids are what deliciousness is all about.

Glycine and alanine have a sweet taste, valine and leucine have a bitter taste, and aspartic acid and glutamate have sour and Umami tastes. Though called a bitter amino acid, valine has a slightly sweet taste as well. The sweetness of glycine and alanine is lighter than that of sugar. Combination of amino acids with their respective tastes is a key determinant for the taste of food. Relationships between amino acids and taste have been explored since the discovery of glutamate as an Umami ingredient.

Determination of amino acids contained in foods revealed that the taste we perceive largely depends on the kinds and amounts of the amino acids.



Umami and sour tastes

Glutamate
Aspartic acid

Sweet taste

Glycine
Alanine
Threonine
Proline
Serine
Glutamine

Bitter taste

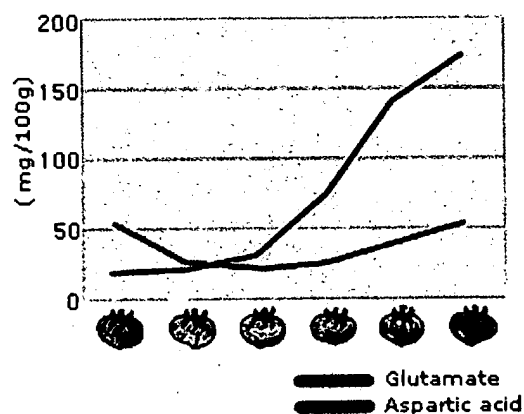
Phenylalanine
Tyrosine
Arginine
Leucine
Isoleucine
Valine
Methionine
Histidine

■ The reason why vine-ripened tomatoes taste good

The taste of tomato mainly consists of two amino acids, organic acids, and sugars. The two amino acids, glutamate and aspartic acid, are essential to the taste of tomato. The ratio of the two amino acids is also important - a glutamate-to-aspartic acid ratio of 4:1 makes the tomato taste the best and brings out the genuine tomato taste.

Young tomato plants bloom with yellow flowers in early summer and then bear small green fruits. Amino acids, together with sugars, increase in amount during the red-ripening process under plenty of sunshine (Figure). If glutamate is removed from the taste of tomato, it tastes like a diluted apple juice or sour.

Glutamate and aspartic acid in tomato





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■ Tastes of crab and sea urchin also come from amino acids.

The taste of snow crab consists of just a few kinds of amino acids, nucleic acids, and minerals (Figure). Each

of them plays a role of its own. For example, arginine, though a bitter amino acid, brings out a seafood-like flavor, and the Umami of glutamate makes the crab taste like a crab. The taste of sea urchin mainly consists of 5 amino acids (Figure). If you mix these 5 amino acids in the same proportions as in a living sea urchin, the taste of sea urchin can be excellently reproduced. Methionine, a very bitter amino acid, is the key ingredient for the taste of sea urchin. Without methionine, sea urchins taste like shrimps or crabs.

Tastes of snow crab and sea urchin

Taste of snow crab Essential ingredients		Taste of sea urchin Essential ingredients	
Amino acids Glycine Alanine Arginine Glutamate		Amino acids Glycine Alanine Glutamate Valine Methionine	
Minerals Sodium Potassium	Nucleic acid related substances Adenylic acid Guanylic acid		Nucleic acid related substances Inosinic acid Guanylic acid

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■ Fermented food is a treasure house of amino acids.

Human beings have long developed various techniques for harvesting, growing, and preserving food in large amounts. In addition to just storage, we have created dietary culture to eat better by putting some good ideas to cooking and processing.

Among them are fermented foods. Although proteins have no tastes of their own, soybean, fish, and milk proteins are degraded by fermentation to amino acids, producing a wide variety of tastes. Typical fermented foods include miso and soy sauce in Japan, fish sauce and paste in Southeast Asia, and cheese and anchovy in Europe. In addition, there are fermented beans called dawadawa and soumbara in Africa and other traditional fermented foods in other regions.

Fermented foods, easy to preserve and full of enriched tastes, are a treasure house of amino acids. They serve as flavor enhancer and seasoning and make food in each place delicious, unique, and special.

□SB"□(JVVarious fermented foods in the world

Japan	Miso, soy sauce (soybean)	Malaysia	Budu (fish)
China	Douchi (soybean)	Indonesia	Terasi (shrimp)
Thailand	Nann pla (fish)	Europe	Cheese (milk)
the Philippines	Patis (fish)	West Africa	Dawadawa (parkia bean)
Myanmar	Nga-pi (fish)	West Africa	Soumbara (parkia bean)

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■ The world's first non-fattening sweetener has made its debut!

Combination of amino acids with unique tastes of their own infinitely expands the possibility of a new taste or function.

Aspartic acid has a sour taste and slight Umami, while phenylalanine has a bitter taste. However, aspartame, a conjugate of the two amino acids, is 200 times as sweet as sugar.

Metabolized as an amino acid in the body, aspartame helps cut down on calorie intake and has no effect on blood glucose level, although it has a natural taste similar to sugar. Therefore, this sweetener is widely used for various purposes such as calorie control for healthy diet and nutrition control in diabetics.

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Good timing in eating meat or raw fish

The wild lion first eats the pancreas, small intestines, and liver of its prey. These organs are delicious because they are richer in amino acids than muscle portions. Two or three days after the lion has left, other animals such as the hyena come to eat the muscle portions of the prey. Around that time, the meat tastes much better since muscle proteins and ATP are increasingly degraded to amino acids and nucleotides (such as inosinate and guanylate). It is also said that raw fish does not taste good when it is too fresh. The reason is the same. Umami of fish reaches its peak about 12 to 24 hours after killing because of increases in amino acid and nucleotide content.

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